

CLAIMS

1. Apparatus for treating tissue specimens by immersion in a liquid, the apparatus comprising a first structure providing a chamber for holding the liquid, and a second structure including holding means for releasably holding the specimens, the first and second structures being relatively moveable in a direction having a vertical component between a first position in which the holding means are relatively close to the chamber and in which the second structure closes the top of the chamber to enable the specimens to be immersed in the liquid whilst the latter is protected from the environment, and a second position in which the holding means are relatively distant from the chamber to enable the specimens to be loaded onto or unloaded from the holding means.
2. Apparatus according to claim 1, wherein the first structure is stationary and the second structure is shiftable vertically with respect to the first structure.
3. Apparatus according to claim 1 or 2, wherein the holding means include magnets to enable specimens, each provided with a metal mount, to be detachably retained on the second structure by magnetic attraction.
4. Apparatus according to any of the preceding claims, wherein the chamber is in the form of an annular trough.
5. Apparatus according to claim 4, wherein the holding means hold the specimens so that the latter depend from the holding means at angularly spaced positions around a circle such that the specimens are lowered into the trough as the second structure is lowered to its first position.

6. Apparatus according to claim 4 or 5, wherein the second structure includes a lid which acts to close the chamber in the first position and the underside of which carries the holding means.
7. Apparatus according to any of the preceding claims, wherein the second structure is rotatably moveable around a central vertical axis, enabling specimens to be loaded onto and unloaded from the second structure at a chosen position alongside the apparatus, either by a robotic arm or a human hand.
8. Apparatus according to any of the preceding claims, wherein the apparatus has the facility to change the liquid when in the first position, enabling the specimens to be treated by different liquids in a succession of treatment stages, whilst retaining the chamber closed.
9. A method of treating tissue specimens by immersion in a liquid in a chamber, the method comprising loading the specimens onto a holder so that the specimens depend from the holder and are disposed above the liquid in the chamber, effecting relative movement between the chamber and the specimens in one direction to cause immersion of the specimens in the liquid whilst maintaining the chamber closed and protected from the environment during immersion, effecting relative movement between the chamber and the specimens in the opposite direction to bring the specimens out of the liquid, and unloading the treated specimens from the holder.
10. A method according to claim 9, wherein the specimens are treated by different liquids in a plurality of treatment stages.
11. A method according to claim 10, wherein the treatment stages are carried out by successive emptying and filling of the chamber with the different liquids, whilst the specimens remain in the chamber and whilst the chamber remains closed and protected from the environment.

12. A method of performing any one or more of the analyses or procedures listed hereunder comprising use of a method or apparatus according to any of claims 1 to 11:

Analysis of the structure of biological tissues.

Analysis of the function of biological tissues.

Analysis of the shapes of biological tissues.

Analysis of the distribution of cell types within biological tissues.

Analysis of the distribution of gene activity within biological tissues,
including the distribution of:

- RNA transcripts
- proteins

Analysis of the distribution of transgenic gene activity within biological tissues,

Analysis of the distribution of cell activities within biological tissues,
including:

- Cell cycle status including arrest
- Cell death
- Cell proliferation
- Cell migration

Analysis of the distribution of physiological states within biological tissues.

Analysis of the results of immunohistochemistry staining techniques.

Analysis of the results of in-situ hybridisation staining techniques.

Analysis of the distribution of molecular markers within biological tissues,
including any coloured or light-absorbing substances, such as:

5,5'-dibromo-4,4'-dichloro-indigo (or other halogenated indigo compounds)
formazan

or other coloured precipitates generated through the catalytic activity of enzymes
including: b-galactosidase, alkaline phosphatase or other coloured precipitates formed upon
catalytic conversion of staining substrates,

including: Fast Red, Vector Red

And including any light-emitting substances,

Therefore including any fluorescent substances,

such as: Alexa dyes, FITC, rhodamine,
And including any luminescent substances,
such as green fluorescent protein (GFP) or similar proteins,
And including any phosphorescent substances.

Analysis of tissues from all plant species.

Analysis of any tissue for agricultural research,
including:

- basic research into all aspects of plant biology (genetics, development, physiology, pathology etc.)
- analysis of tissues which have been genetically altered.

Analysis of tissues from all animal species.

including:

- invertebrates

- nematode worms

- vertebrates

- all types of fish (including teleosts, such as zebrafish, and chondrycthes including sharks)

- amphibians (including the genus *Xenopus* and axolotls)

- reptiles

- birds (including chickens and quails)

- all mammals (including all rodents, dogs, cats and all primates, including human)

Analysis of embryonic tissues for any purpose,

including:

- research into any stem cell population

- research into developmental biology

- research into the causes of abnormal embryo development, including human syndromes

autopsies of human terminated pregnancies (both spontaneous and induced terminations)

Analysis of any tissues for the purpose of genomics research,
including:

the analysis of any tissues for the purpose of genomics research,

including:

the analysis of transgenic, knock-in, knock-down or knock-out organisms

the analysis or discovery of the expression (or activity) of genes including their spatial distribution, and their levels of expression

the analysis or discovery of abnormalities in the structure or morphology of tissues, as a result of interference due to wilful experimentation (such as genetic or physical modifications including a chemical or biochemical genomics approach), and/or spontaneous abnormalities (such as naturally-occurring mutations)

Analysis of any tissue for the purpose of neurobiology research,
including:

the analysis of the morphology of nerves

the analysis of the pathways and connectivity of nerves

the analysis of parts of, or whole, animal brains

Analysis of any tissue for pharmaceutical research,
including:

the analysis of pharmaceutical substances (such as drugs, molecules, proteins, antibodies),

including their spatial distribution within the tissue, and their concentrations

the analysis or discovery of abnormalities in the structure or morphology of tissues.

Analysis of tissues for medical research,
including:

research into the genetics, development, physiology, structure and function of animal tissues

analysis of diseased tissue to further our understanding of all types of diseases

including:

congenital diseases

acquired diseases

including:

infectious

neoplastic

vascular

inflammatory

traumatic

metabolic

endocrine

degenerative

drug-related

iatrogenic or

idiopathic diseases

Analysis of tissues for medical diagnosis, treatment or monitoring,

including:

the diagnosis of cancer patients

including:

searching for cancerous cells and tissues within biopsies

searching for abnormal structure or morphology of tissues within biopsies

the analysis of all biopsies

including the analysis of:

lymph nodes

polyps

liver biopsies

kidney biopsies

prostate biopsies

muscle biopsies

brain tissue

the analysis of tissue removed in the process of extracting a tumour from a patient including:

determining whether all the tumour has been removed

determining the type of tumour, and the type of cancer.

13. Use of a method or apparatus as described in any of claims 1 to 11 in any one or more of the analyses or procedures listed hereunder:

Analysis of the structure of biological tissues.

Analysis of the function of biological tissues.

Analysis of the shapes of biological tissues.

Analysis of the distribution of cell types within biological tissues.

Analysis of the distribution of gene activity within biological tissues,
including the distribution of:

- RNA transcripts
- proteins

Analysis of the distribution of transgenic gene activity within biological tissues,

Analysis of the distribution of cell activities within biological tissues,
including:

- Cell cycle status including arrest
- Cell death
- Cell proliferation
- Cell migration

Analysis of the distribution of physiological states within biological tissues.

Analysis of the results of immunohistochemistry staining techniques.

Analysis of the results of in-situ hybridisation staining techniques.

Analysis of the distribution of molecular markers within biological tissues,
including any coloured or light-absorbing substances, such as:

5,5'-dibromo-4,4'-dichloro-indigo (or other halogenated indigo compounds)
formazan

or other coloured precipitates generated through the catalytic activity of enzymes
including: b-galactosidase, alkaline phosphatase or other coloured precipitates formed upon
catalytic conversion of staining substrates,

including: Fast Red, Vector Red

And including any light-emitting substances,

Therefore including any fluorescent substances,

such as: Alexa dyes, FITC, rhodamine,

And including any luminescent substances,

such as green fluorescent protein (GFP) or similar proteins,

And including any phosphorescent substances.

Analysis of tissues from all plant species.

Analysis of any tissue for agricultural research,

including:

basic research into all aspects of plant biology (genetics, development, physiology,
pathology etc.)

analysis of tissues which have been genetically altered.

Analysis of tissues from all animal species.

including:

invertebrates

nematode worms

vertebrates

all types of fish (including teleosts, such as zebrafish, and chondrycthes including
sharks)

amphibians (including the genus *Xenopus* and axolotls)

reptiles

birds (including chickens and quails)

all mammals (including all rodents, dogs, cats and all primates, including human)

Analysis of embryonic tissues for any purpose,
including:

- research into any stem cell population
- research into developmental biology
- research into the causes of abnormal embryo development, including human syndromes
- autopsies of human terminated pregnancies (both spontaneous and induced terminations)

Analysis of any tissues for the purpose of genomics research,
including:

- the analysis of any tissues for the purpose of genomics research,
including:

- the analysis of transgenic, knock-in, knock-down or knock-out organisms
- the analysis or discovery of the expression (or activity) of genes including their spatial distribution, and their levels of expression
- the analysis or discovery of abnormalities in the structure or morphology of tissues, as a result of interference due to wilful experimentation (such as genetic or physical modifications including a chemical or biochemical genomics approach), and/or spontaneous abnormalities (such as naturally-occurring mutations)

Analysis of any tissue for the purpose of neurobiology research,
including:

- the analysis of the morphology of nerves
- the analysis of the pathways and connectivity of nerves
- the analysis of parts of, or whole, animal brains

Analysis of any tissue for pharmaceutical research,
including:

the analysis of pharmaceutical substances (such as drugs, molecules, proteins, antibodies),
including their spatial distribution within the tissue, and their concentrations
the analysis or discovery of abnormalities in the structure or morphology of tissues.

Analysis of tissues for medical research,

including:

research into the genetics, development, physiology, structure and function of
animal tissues

analysis of diseased tissue to further our understanding of all types of diseases

including:

congenital diseases

acquired diseases

including:

infectious

neoplastic

vascular

inflammatory

traumatic

metabolic

endocrine

degenerative

drug-related

iatrogenic or

idiopathic diseases

Analysis of tissues for medical diagnosis, treatment or monitoring,

including:

the diagnosis of cancer patients

including:

searching for cancerous cells and tissues within biopsies

searching for abnormal structure or morphology of tissues within biopsies
the analysis of all biopsies

including the analysis of:

lymph nodes

polyps

liver biopsies

kidney biopsies

prostate biopsies

muscle biopsies

brain tissue

the analysis of tissue removed in the process of extracting a tumour from a patient
including:

determining whether all the tumour has been removed

determining the type of tumour, and the type of cancer.